B 25

(12) UK Patent Application (19) GB (11) 2 178 658 A

(43) Application published 18 Feb 1987

(21) Application No 8618212

(22) Date of filing 25 Jul 1986

(30) Priority data
(31) 8518927 (32) 26 Jul 1985 (33) GB

(71) Applicant
Vincent Processes Limited

(Incorporated in United Kingdom)

Turnpike Road Industrial Estate, Shaw, Newbury, Berks RG13 2NT

(72) Inventor
Maurice William Vincent

(74) Agent and/or Address for Service
Eric Potter & Clarkson,
27 South Street, Reading, Berks RG1 4QU

(51) INT CL⁴
A61K 9/22 47/00

(52) Domestic classification (Edition I):
A5B 180 828 830 835 M N
U1S 1330 1580 A5B

(56) Documents cited
GB A 2152940 GB 1113860 GB 0934089
GB 1390311 GB 1097207 EP A2 0068450
GB 1263392

(58) Field of search
A5B
Selected US specifications from IPC sub-class A61K

(54) Sustained release tablets and a method of manufacture thereof

(57) A slow release tablet comprising an excipient, one or more active agents, and a polymeric material, is prepared by substantially uniformly distributing the active agent throughout the excipient and the polymeric material, (eg. by melting and mixing) and then forming the mixture into tablets.

The excipient may be one or more starches or sugars, the polymeric material is suitably polyvinyl pyrrolidone or polyvinyl chloride.

GB 2 178 658 A

SPECIFICATION

Tablets and a method of manufacture thereof

This invention relates to tablets and a method of manufacturing the same, the term "tablet" as used throughout this specification and claims includes sweets and lozenges as well as tablets per se. More particularly, the invention is concerned with slow release tablets, i.e. tablets from which the specific is released in a controlled manner. By "specific" is meant, throughout this specification and claims, the actual drug or other component(s) of the tablet formulation which exert the desired effect which may be a pharmacological effect in the case of treatment of humans or animals. However, the invention is applicable to other types of tablets for use, for example, in the agrochemical field.

In the treatment of an illness or condition by administration of tablets, the pharmacological effect results from the ingestion of the tablet followed by dispersion of the specific through the stomach wall into the human or animal body.

In many instances, the presentation of the specific to the body should ideally be delayed so as to prolong the treatment time. In some cases, the specific should not be made available to the body until it has passed through the stomach. Delayed release characteristics are currently implemented by enclosing the specific within a soluble capsule, the rate of dissolution of the capsule determining the delay, from the instant of swallowing, in the availability of the specific to the human or animal body. One of the disadvantages of this technique is that once the capsule has dissolved, the entire contents of the capsule become available for assimilation and this can have adverse side effects in that a localised high concentration of a specific is not always acceptable to the digestive system and can lead to internal irritation and, in severe cases, to internal haemorrhage.

The present invention seeks to provide a slow release tablet from which the release of the specific is controlled in a manner superior to that known at present.

According to the present invention, a tablet comprises a base material, one or more specifics, and a polymeric material, the or each specific being substantially uniformly distributed throughout the base material and the polymeric material.

Further according to the present invention there is provided a method of manufacturing a tablet comprising the steps of preparing a melt of a base material and a polymeric material, adding one or more specifics, forming these ingredients into a substantially homogenous mixture, and cooling.

If the tablet is to be in the form of a sweet, the method comprises the further step, prior to the cooling step, of moulding the homogeneous melt into the required shape and size of sweet. If the tablet is to be in the form of an actual tablet, the method comprises the still further steps of grinding the cooled melt into a powder, and forming the powder into tablets, possibly with the prior or subsequent inclusion of further ingredients such as conventional tableting agents. If the tablet is to be in the form of a lozenge, the melt may include a mucilaginous material.

The base material is essentially a carrier and diluent and may comprise ingredients normally used in tableting and confectionery preparations. These may include colourants and flavourants although these may be added at the actual tableting stage when appropriate.

The melt may be formed using either the techniques employed in conventional sugar confectionery processing or the technique of extrusion cooking, the latter being preferred because nearly dry ingredients can be used for the melt without the need to add and then remove significant quantities of water which has to be done in the conventional evaporative processes used in confectionery manufacture. Another advantage of employing extrusion cooking is that thermal degradation of any thermally-sensitive ingredient, especially the or each specific, is minimised.

The crux of the present invention lies in the use of a polymeric material which, when the product is for in vivo use, may be in the form of a non-biodegradable, but biologically compatible, polymeric material, such as PVP. When the product is for a non-medical application, the polymeric material may be biodegradable or non-biodegradable but does not need to be biologically compatible and such a non-biodegradable material is PVC. For medical or non-medical application, a biodegradable polymeric material such as starch polymer may be employed. The role of the polymeric material, which has the or each specific substantially uniformly distributed therein, is to slow down the release of the or each specific into the human body, animal body or the environment, as applicable. It will be appreciated that the choice of base material and the relative proportions of base material and polymeric material will determine the amount of the or each specific which is released relatively quickly on dissolution of the base material and that which is released comparatively slowly from the polymeric material.

Thus a relatively fine control of the release of one or more specifics is afforded by the present invention which represents a significant advance in the art. This is because not only are the problems of irritation and haemorrhaging referred to above overcome by avoiding high local concentrations of a specific but the improved slow release characteristic is far better suited to certain medications.

The invention will now be described in greater detail, by way of illustration, with reference to the following examples.

Example 1

Tablets in the form of actual tablets are produced first by extrusion cooking a mixture, cooling that mixture, grinding the cooled mixture to a powder, and then forming the powder into tablets using conventional tableting techniques.

More specifically, the mixture comprises a base material and a polymeric material which are loaded in basically dry form into the extrusion cooker in the required proportions by weight which are determined by the desired release characteristics to be imparted to the tablets. The base material may include, among other ingredients, the following:–

Lactose and/or other sugars
Modified Starches
Unmodified Starches
Maltodextrins
Sodium and/or Calcium and/or Magnesium Stearates
Colourant(s)
Flavourant(s)

The polymeric material may be PVP if a non-biodegradable material is required, or a polymerised starch if a biodegradable material is required.

The mixture of base material and polymeric material is then worked under elevated temperature and pressure, in the normal way of extrusion cooking, so as to reduce the mixture to a melt, whereby the polymeric material forms a continuum or matrix. The melt is extruded through a die head but at a point immediately behind the die head, in a zone of relatively high shear, one or more specifics is or are injected into the melt. The shear to which the melt is subjected at the chosen injection point of the or each specific is sufficiently high to ensure substantially uniform distribution of the or each specific throughout the melt of base material and polymeric material. If any of the ingredients of the base material are thermo-sensitive, these too can be added just before, with or just after the or each specific. However, if a specific is not thermo-sensitive, this can be added to the mixture of base material and polymeric material at the outset.

The extruded melt is cooled as quickly as possible in order to minimise any thermal degradation of thermo-sensitive ingredients and this cooling may be effected c nventi nally such as by depositing on a cooled, continuously-moving steel band, r on a r tating, chilled roll. In the case of agrochemical applications, cooling may be effected by prilling.

The cooled material is then ground to a fin powder and subsequently formed into tablets using a conventional tableting press. Conv ntional tableting ingredients may be added to the powder before being pressed into tablets.

Example 2

The same selection of base material and polymeric material as Example 1 may be made and these mixed or blended with the required specific or specifics to form an homogenous mixture. To this mixture is added water and the composition then heated to drive the water and so produce a melt, this method being that of a conventional confectionery manufacturing process. The melt is then moulded into the desired size and shape to form sweets and then cooled as rapidly as possible, again to minimise any thermal degradation of one or more ingredients, especially the specific or specifics.

Example 3

As Example 2 but with the cooled material and then ground to a fine powder for tableting as in Example 1, instead of being moulded.

Example 4

As Example 2 but with the base material including a mucilaginous material, whereby the moulded melt formslozenges rather than sweets.

Example 5

In this Example, the base material is based essentially on sugars only, typically lactose, so that the melt mixture comprises sugar, a polymeric material and a specific. The melt may be formed by the extrusion cooking method of Example 1 or the confectionery process of Example 2 and then cooled and ground to a fine powder. Tableting agents such as starches, maltodextrins and stearates, for example, may then be added to the powder and the resulting mixture formed into tablets as in Example 1.

The use of a polymeric material in which part of the or each specific is distributed gives rise, as already explained to a significant advance in the art of slow release tablets. If a biodegradable polymeric material is used, then the specific is released as the polymeric material is broken down but if a non-biodegradable material is used, the or each specific is gradually leached out, or released as the matrix is dissolved.

If a basic delay in the specific release programme is required, perhaps to allow the tablet first to pass through the stomach, or to pass thr ugh a significant proportion of the digestive tract, f r example, then a conventi nal coating may be applied. It will be appreciated that the inv nti n all ws the use of one or more specifics which is advantageous in certain applications.

As already indicated the invention is applicable to tablets for human and animal ingestion and als to oth r tablets which need to have slow release prop rties such as in the

agrochemical field.

CLAIMS

1. A tablet comprising a base material, one or more specifics, and a polymeric material, the or each specific being substantially uniformly distributed throughout the base material and the polymeric material.

2. A tablet according to claim 1, wherein the polymeric material is non-biodegradable, biologically compatible polymeric material.

3. A tablet according to claim 2, wherein the polymeric material is PVP.

4. A tablet according to claim 1, wherein the polymeric material is biodegradable or non-biodegradable and is biologically or non-biologically compatible.

5. A tablet according to claim 4, wherein the polymeric material is non-biodegradable and is PVC.

6. A tablet according to claim 4, wherein the polymeric material is biodegradable and biologically compatible and is a starch polymer.

7. A method of manufacturing a tablet comprising the steps of preparing a melt of a base material, and a polymeric material, adding one or more specifics, forming these ingredients into a substantially homogenous mixture, and cooling.

8. A method according to claim 7 and including the further step of moulding the substantially homogenous melt into a predetermined size and shape.

9. A method according to claim 7 and including the further steps of grinding the cooled melt into a powder and forming the powder into tablets.

10. A method according to claim 9 and including the further step of mixing the powder with one or more tableting agents prior to forming the tablets.

11. A method according to claim 7 or 8 and including the further step of adding a mucilaginous material to the melt.

12. A method according to any of claims 7 to 11, wherein the melt is prepared by extrusion cooking.

13. A method according to claim 12, wherein the or each specific is added to the melt prior to the melt being extruded from the extrusion cooker.

14. A method according to claim 13, wherein the or each specific is added to the melt at a point immediately prior to the melt being extruded through a die head of the extrusion cooker, said point being in a zone of the cooker of relatively high shear.

15. A method according to claim 12 or 13, wherein one or more ingredients of the base material is or are thermo-sensitive and is or are added to the melt immediately prior or post the addition of the or each specific.

16. A method according to any of claims 7 to 15, wherein the cooling step is performed by depositing the melt on a cooled, continuously moving conveyor.

17. A method according to any of claims 7 to 15, wherein the cooling step is performed by depositing the melt on a chilled roll.

18. A method according to any of claims 7 to 15, wherein the cooling step is effected by prilling.

19. A method according to any of claims 7 to 18, and including the further step of applying coating to the tablet.

20. A method of manufacturing a tablet substantially as herein particularly described with reference to Examples 1 to 5 of the specification.

21. A tablet produced according to the method of any of claims 7 to 19.

Printed for Her Majesty's Stationery Office
by Burgess & Son (Abingdon) Ltd, Dd 8817356, 1987.
Published at The Patent Office, 25 Southampton Buildings,
London, WC2A 1AY, from which copies may be obtained.